

PATENT COOPERATION TREATY

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PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

07 June 2000 (07.06.00)

International application No.

PCT/SE99/01687

Applicant's or agent's file reference

103364701

International filing date (day/month/year)

24 September 1999 (24.09.99)

Priority date (day/month/year)

24 September 1998 (24.09.98)

Applicant

PETTERSSON, Anders et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

19 April 2000 (19.04.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Claudio Borton

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY
PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 103364701	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/SE 99/01687	International filing date (<i>day/month/year</i>) 24 Sept 1999	(Earliest) Priority Date (<i>day/month/year</i>) 24 Sept 1998
Applicant Diabact AB et al		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (See Box I).

2. ☐ Unity of invention is lacking (See Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
 - ☐ filed with the international application.
 - ☐ furnished by the applicant separately from the international application,
 - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - ☐ transcribed by this Authority.

4. With regard to the title,
 - ☐ the text is approved as submitted by the applicant.
 - ☒ the text has been established by this Authority to read as follows:

Pharmaceutical composition for the treatment of acute disorders.

5. With regard to the abstract,
 - ☒ the text is approved as submitted by the applicant.
 - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. _____

 - ☐ as suggested by the applicant.
 - ☐ because the applicant failed to suggest a figure.
 - ☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE99/01687

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **19-21**
because they relate to subject matter not required to be searched by this Authority, namely:
See extra sheet.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE99/01687

Claims 19-21 relates to methods of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/ Rule. 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compound(s)/composition(s).

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 99/01687

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 9/16, A61K 31/445 // A61K 31/44, A61K 31/34, A61K 38/16, A61K 31/19
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0324725 A1 (KABIVITRUM AB), 19 July 1989 (19.07.89) --	1-21
A	Dialog Information Services, File 154, MEDLINE, Dialog accession no. 09481986, Medline accession no. 98213107, Farrar JT et al: "Oral transmucosal fentanyl citrate: randomized, double-blinded, placebo-controlled trial for treatment of break- through pain in cancer patients"; J Natl Cancer Inst (UNITED STATES) Apr 15 1998, 90 (8) p 611-6, see abstract --	16,18
A	EP 0144243 A1 (RECKITT AND COLMAN PRODUCTS LIMITED), 12 June 1985 (12.06.85) -- -----	1-21

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document but published on or after the international filing date	"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 12 January 2000	Date of mailing of the international search report 22 -01- 2000
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Anneli Jönsson/ELY Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT
Information on patent family members

02/12/99

International application No.
PCT/SE 99/01687

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0324725 A1	19/07/89	AT 87467 T	15/04/93
		AU 2923389 A	11/08/89
		DE 6890561 U	06/05/93
		DE 68905613 T	07/10/93
		DK 585088 A	20/10/88
		EP 0396599 A	14/11/90
		FI 893810 D	00/00/00
		NO 884723 A	24/10/88
		SE 8800080 A	14/07/89
		WO 8906533 A	27/07/89
EP 0144243 A1	12/06/85	SE 0144243 T3	
		AU 569930 B	25/02/88
		AU 3632984 A	13/06/85
		CA 1234353 A	22/03/88
		DK 163711 B,C	30/03/92
		DK 577984 A	07/06/85
		GB 2150832 A,B	10/07/85
		GR 81186 A	08/04/85
		IE 57876 B	05/05/93
		JP 1780447 C	13/08/93
		JP 4069605 B	06/11/92
		JP 60146824 A	02/08/85
		NZ 210442 A	29/02/88
		PT 79615 A,B	01/01/85
		US 4582835 A	15/04/86

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ :A61K 9/16, 31/445 // 31/44, 31/34, 38/16,
31/19

A1

(11) International Publication Number:

WO 00/16750

(43) International Publication Date:

30 March 2000 (30.03.00)

(21) International Application Number: PCT/SE99/01687

(22) International Filing Date: 24 September 1999 (24.09.99)

(30) Priority Data:

9803240-2

24 September 1998 (24.09.98) SE

(71) Applicant (for all designated States except US): DIABACT AB
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(72) Inventors; and

(75) Inventors/Applicants (for US only): PETTERSSON, An-
ders [SE/SE]; Knaverstad 13060, S-442 97 Kode (SE).
NYSTRÖM, Christer [SE/SE]; Holmvägen 22 B, S-756 61
Uppsala (SE).(74) Agents: HANSSON, Sven, A. et al.; AB Stockholms Patent-
byrå, Zacco & Bruhn, Box 23101, S-104 35 Stockholm
(SE).(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG,
BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE,
ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS,
MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

With amended claims.

(54) Title: PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF ACUTE DISORDERS

(57) Abstract

A pharmaceutical composition for the treatment of acute disorders is described. The composition comprises an essentially water-free, ordered mixture of at least one pharmaceutically active agent in the form of microparticles which are adhered to the surfaces of carrier particles which are substantially larger than the particles of the active agent or agents, and are essentially water-soluble, in combination with the bioadhesion and/or mucoadhesion promoting agent. The invention also relates to a method for preparing the composition and to the use of the composition for the treatment of acute disorders.



PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 103364701/SAH	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/SE99/01687	International filing date (<i>day/month/year</i>) 24.09.1999	Priority date (<i>day/month/year</i>) 24.09.1998
International Patent Classification (IPC) or national classification and IPC ₇ A61K 9/16, A61K 31/445//A61K 31/44, A61K 31/34, A 61K 38/16, A61K 31/19		
Applicant Diabact AB et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 19.04.2000	Date of completion of this report 16.01.2001
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 08-667 72 88	Authorized officer Henrik Nilsson/EÖ Telephone No. 08-782 25 00

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE99/01687

I. Basis of the report1. With regard to the **elements** of the international application:*

- ☐ the international application as originally filed
- ☒ the description:
pages 1-15, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement) under article 19
pages _____, filed with the demand
pages 16-18, filed with the letter of 11.01.2001
- ☒ the drawings:
pages 1, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheet/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2 (c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE99/01687

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 19-21

because:

☒ the said international application, or the said claims Nos. 19-21

relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/se99/01687

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	<u>1-18</u>	YES
	Claims	_____	NO
Inventive step (IS)	Claims	<u>1-18</u>	YES
	Claims	_____	NO
Industrial applicability (IA)	Claims	<u>1-18</u>	YES
	Claims	_____	NO

2. Citations and explanations (Rule 70.7)

The invention relates to a pharmaceutical composition for sublingual administration in the treatment of acute disorders, such as pain or allergic conditions. The composition comprises an essentially water-free "ordered mixture" of microparticles, which are adhered to the surfaces of carrier particles. The carrier particles are substantially larger than the microparticles, and are essentially water-soluble. The composition also comprises a bioadhesion- or a mucoadhesion-promoting agent mainly adhered to the surfaces of the carrier particles. In one embodiment fentanyl or a pharmaceutically acceptable salt thereof is used as an active agent.

The International Search revealed the following documents of particular relevance:

- A. EP324725 A1
- B. Farrar JT et al. J Natl Cancer Inst 90 (1998), 611-616 (MEDLINE-abstract)
- C. EP144243 A1

.../...

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE99/01687

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: V

Document A discloses an essentially water-free composition comprising an ordered mixture of water-soluble particles and significantly smaller particles of the active substance. The active substance particles adhere to the surface of the carrier particles. In the composition disclosed in document A, the concentration of active substance is 0.4-5% by weight. The active substance particles are smaller than 10 μm in diameter and the carrier particles have a diameter of 100-500 μm . The carrier particles consist of mannitol or lactose and therefore fragmentize easily when compressed, for instance in the manufacture of tablets. The carrier particles also comprise up to 25% modified cellulose gum, which functions as disintegrant and facilitates dissolution of the carrier particles and release of the active substance. However, in the pharmaceutical composition disclosed in document A, fentanyl is not used as active substance, and the document only discloses oral, not sublingual, administration of the composition. Furthermore, no surfactant has been used in the composition known through document A. Cellulose gum has been used in document A, however without disclosing its function as a bioadhesion agent. In document A, the cellulose gum is evenly distributed in the carrier particles, thus being present on the surfaces of the carrier particles as well as inside the particles.

Document B discloses oral transmucosal administration of a salt of fentanyl for treatment of acute pain.

Document C discloses sublingual administration of the analgesic substance buprenorphine, which is one active substance suggested in the present application.

None of the documents revealed in the International Search relate to sublingual administration of an ordered mixture. Furthermore, the documents do not suggest the use of a bioadhesion or mucoadhesion agent mainly adhered to the surfaces of the carrier particles. Particular advantages, such as reduced erratic drug absorption, are obtained by the pharmaceutical composition of the present invention. Thus, claims 1-18 are considered to fulfil the requirements of novelty, inventive step and industrial applicability.